Version of Amended Specification Paragraphs With Markings to Show Changes Made:

NOTE: Deletions are marked by brackets and bold text.

Paragraph 1:

Transporters are generally classified by structure and the type of mode of action. In addition, transporters are sometimes classified by the molecule type that is transported, for example, sugar transporters, chlorine channels, potassium channels, etc. There may be many classes of channels for transporting a single type of molecule (a detailed review of channel types can be found at Alexander, S.P.H. and J.A. Peters: Receptor and transporter nomenclature supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 (1997) **[and http://www-biology.ucsd.edu/~msaier/transport/titlepage2.html]**.

Paragraph 2:

Ion channels are generally classified by structure and the type of mode of action. For example, extracellular ligand gated channels (ELGs) are comprised of five polypeptide subunits, with each subunit having 4 membrane spanning domains, and are activated by the binding of an extracellular ligand to the channel. In addition, channels are sometimes classified by the ion type that is transported, for example, chlorine channels, potassium channels, etc. There may be many classes of channels for transporting a single type of ion (a detailed review of channel types can be found at Alexander, S.P.H. and J.A. Peters (1997). Receptor and ion channel nomenclature supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 **[and http://www-biology.ucsd.edu/~msaier/transport/toc.html]**.

Paragraph 3:

The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm. (*Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data, Part 1*, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and

Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package **[(available at http://www.gcg.com)]**, using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereux, J., *et al., Nucleic Acids Res. 12(1)*:387 (1984)) **[(available at http://www.gcg.com)]**, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Myers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

Paragraph 4:

DESCRIPTION OF THE FIGURE SHEETS

FIGURE 1 (FIGURE SHEETS 1A-1B) provides the nucleotide sequence of a cDNA molecule or transcript sequence that encodes the transporter protein of the present invention. In addition structure and functional information is provided, such as ATG start, stop and tissue distribution, where available, that allows one to readily determine specific uses of inventions based on this molecular sequence. Experimental data as provided in FIGURE 1 indicates expression in the fetal liver and spleen.

FIGURE 2 (FIGURE SHEETS 2A-2B) provides the predicted amino acid sequence of the transporter of the present invention. In addition structure and functional information such as protein family, function, and modification sites is provided where available, allowing one to readily determine specific uses of inventions based on this molecular sequence.

FIGURE 3 (FIGURE SHEETS 3A-3TT) provides genomic sequences that span the gene encoding the transporter protein of the present invention. In addition structure and functional information, such as intron/exon structure, promoter location, etc., is provided where available,

allowing one to readily determine specific uses of inventions based on this molecular sequence. 55 SNPs, including 4 indels, have been identified in the gene encoding the transporter protein provided by the present invention and are given in Figure 3.

Version of Amended Claims With Markings to Show Changes Made:

24. (Amended) A process for producing a polypeptide comprising SEQ ID NO:2, the process comprising culturing the host cell of claim 9 under conditions sufficient for the production of said polypeptide, and recovering said polypeptide from the host cell culture, wherein said isolated nucleic acid molecule encodes a polypeptide comprising SEQ ID NO:2.

28. (Amended) A vector according to claim 8, wherein said isolated nucleic acid molecule encodes a polypeptide comprising SEQ ID NO:2 and is inserted into said vector in proper orientation and correct reading frame such that a polypeptide comprising [the protein of] SEQ ID NO:2 may be expressed by a cell transformed with said vector.

REMARKS

Applicants have studied the Office Action mailed Octorber 15, 2002. Reconsideration and allowance of the pending claims in view of the above amendments and the following remarks is respectfully requested.

Drawings:

The Examiner states that the instant specification does not comply with 37 C.F.R. § 1.84(U)(1) because drawings contained on multiple sheets, which are intended to form one complete view, must be identified by the same number followed by a capital letter.

In response, Applicants submit formal drawings herewith, having correct numbering of drawing sheets.

Specification:

The Description to the drawings has been changed accordingly as set forth above. Figure 1 has been changed with insertion of Figure sheets 1A –1B, Figure 2 has been changed with insertion of Figure sheets 2A-2B, and Figure 3 has been changed with insertion of Figure sheets 3A-3TT.

Hyperlinks:

The Examiner objected to the disclosure as containing embedded hyperlinks and/or other browser-executable code.

In response, Applicants have deleted all hyperlinks from the specification, as indicated above by the replacement paragraphs.

Listing of references:

The Examiner stated that the listing of references in the specification is not a proper information disclosure statement. The Examiner states that, unless the references have been cited on form PTO-892, they have not been considered.

In response, Applicants acknowledge that the references listed in the specification are incorporated by reference pursuant to MPEP §608.01(p) and, to be considered by the Examiner, references must be cited as a proper information disclosure statement on form PTO-892.

Rejection under 35 U.S.C. §101 and 35 U.S.C §112, first paragraph:

At page 3 of the Office Action, the Examiner has rejected the claims 4, 8-9, 13 and 24-25, 27-29 under 35 U.S.C.§101/112. In summary, the Examiner has stated that the claimed isolated nucleic acid molecules lack utility because Applicants have failed to point out a specific use.

The Examiner stated that, because the specification has failed to credibly identify a physiological process which has been shown to be influenced by the activation or inhibition of a putative transporter protein of the instant invention, an artisan would have no way of predicting what effects the administration of an agonist or antagonist thereto to an organism would have (page 4 first paragraph).

The Examiner further stated that the instant specification fails to disclose any relationship between orphan transport in the disorders. The Examiner further stated that the actual and specific significance is required to the transporter protein described in the specification, or the invention would be incomplete (page 5, second paragraph).

Applicants respectfully traverse this rejection based on the following remarks.

The utility requirement of a claimed invention requires that an invention must have a specific, substantial and credible utility. These requirements are defined in broad terms in cases such as *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) and the recently adopted Utility Guidelines from the USPTO.

The CCPA in *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980), clearly accepted a showing of less than a specific therapeutic use of a claimed chemical compound as satisfying the utility requirement.

> *The CCPA held that where a claim does not provide evidence of pharmacological activity of a claimed compound, although it does not establish a specific therapeutic use, manifests a practical utility because knowledge of pharmacological activity is beneficial to the public in that it makes faster and easier for medical researchers to combat illnesses. Nelson v. Bowler, 206 USPQ 881 (CCPA 1980).*

The notion that a recognized valuable addition to even entry points of the drug discovery cycle advances the art sufficient to establish a "usefulness" of a claimed invention should not be ignored. Similar to the *Nelson* case, the present invention, which is drawn to isolated nucleic acid molecules that encode a transporter protein (SEQ ID NO: 2), has useful value in the drug discovery process even though the molecule may not be associated with a specific treatment and/or diagnosis of a particular disease. According to *Nelson*, the present invention provides sufficient knowledge and information that is beneficial to the public, and provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. It is well recognized that transporters are the most important targets for drug action (pages 1-14 of the specification). The public disclosure of a new member of this family through the patenting process clearly advances the art and augments the capabilities of biomedical researchers to combat illnesses.

The utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). *Juicy Whip* held that, in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful result." The polypeptides and encoding nucleic acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc. In addition to the uses disclosed in the specification and discussed herein for the polynucleotides of the present invention, other utilities are readily apparent to one of ordinary skill in the art based on the observed tissue specific expression patterns. Specifically, the proteins/nucleic acid molecules of the present invention are expressed in leukocyte. Thus, for example, the proteins/nucleic acids of the present invention are commercially useful for developing therapeutic agents for treating diseases affecting these tissues. Therefore, the present invention is not "totally incapable of achieving a useful result." Instead, it is useful.

The specification and figures show that the protein of the present invention has functional domains of calcium-binding transporter. The disclosure of the function of calcium-binding transporter is sufficient. Such a function is quite specific for transporter proteins and differentiates them from other proteins. As such, this function is specific enough to define a use for novel transporter proteins and transporter-encoding nucleic acid molecules in the drug discovery process.

As stated in the Background section of the specification, the protein of the present invention is very similar to the calcium-binding transporters, which is related to the mitochondrial solute carrier proteins subfamily in general and the peroxisomal calcium-dependent solute carrier subfamily in particular. Mitochondrial solute carrier proteins are found at the mitochondrial innter membrane and are important for metabolite transport across the membrane. Therefore, the novel protein of the present invention, i.e. mitochondrial solute carrier proteins/genes are medically and commercially useful for diagnosing and/or treating mitochondrial-associated diseases/disorders.

Novel transporter proteins/nucleic acids are commercially useful for developing therapeutics/diagnostics for these and other pathologies. Thus, there is overwhelming evidence in the art to support the utility of novel transporter proteins and encoding nucleic acid molecules, particularly those related to calcium-binding transporter. Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the transporter family of proteins, even though each member may play a somewhat different role in cellular responses and pathologies. Even though each member may have a somewhat different role in biology and disease, each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

By placing a new member of the transporter protein family into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further discovery. The Utility requirement cannot be used to contradict the reasons for the patent system, to encourage early disclosures of inventions so that others can benefit from, improve upon, and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new transporter proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

The grant of a patent to the claimed isolated nucleic acid molecule and the resultant disclosure of the nucleic acid and protein sequences to the public will certainly shorten the process for medical researchers to discover other novel uses for the present transporter-encoding nucleic acids. One example disclosed in the specification is that the present nucleic acid

molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents can be used to precisely determine which biological and pathological processes the protein is involved in. Furthermore, such agents that bind to a protein target and modulate cell signaling may subsequently be developed and refined for use in mammalian therapeutic applications. All of this later discovery and refinement will be done using the presently claimed material. These uses are clearly commercial and substantial uses that are specific for a very limited number of proteins/nucleic acid molecules.

In addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112, first paragraph. The claimed invention is directed to nucleic acid sequences that encode a transporter protein with a specified amino acid sequence (SEQ ID NO: 2), such as SEQ ID NOS: 1 and 3. Exemplary uses of the nucleic acid sequences are clearly recited in the specification on, for example, pages 37-60. Among the examples, the nucleic acid molecules are useful as hybridization probes for messenger RNA molecules, transcript/cDNA molecules, genomic DNA, and variants thereof. An expression vector comprising the nucleic acid sequences can be made that expresses the transporter protein. Such uses are specific for the claimed nucleic acid molecules, and the products of such uses will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different nucleic acid molecule for the same purpose.

In view of law and fact, the utility standard interpreted by the USPTO guidelines is too high. The disclosure of activity of the expressed polynucleotide is not required by any statute or case law interpreting the utility requirement of Section 101, and the enablement requirement of Section 112, first paragraph. The commercial value of a gene that encodes a previously unidentified member of the transporter protein family, members of which are well known in the art to be commercially valuable drug targets, should be sufficient to satisfy the utility requirement.

Rejection of claims 24, 28, and 29 under 35 USC §112, 2nd paragraph:

The Examiner rejected claim 24 as being vague and indefinite because the identity of the polypeptide being produced is not indicated (because thousands of different polypeptides can be

produced by culturing a host cell). The Examiner also rejected claims 24, 28, and 29 as being incomplete because they are not limited to an isolated nucleic acid molecule encoding a polypeptide due to their ultimate dependence on part (d) of claim 4.

In response, Applicants have amended claim 24 to clarify that the polypeptide that is intended to be produced is a polypeptide comprising SEQ ID NO:2, and to clarify that the claimed process is intended to be limited to a process that employs a nucleic acid molecule that encodes a polypeptide. Additionally, Applicants have amended claim 28 to clarify that the claimed vector contains a nucleic acid molecule that encodes a polypeptide. Claim 29 is dependent on claim 28 and therefore clarified by way of the amendment to claim 28.

Thus, in view of these amendments and remarks, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 24, 28, and 29 under 35 USC §112, second paragraph.

Conclusions

Claims 4, 8-9, and 24-29 are currently pending. The amendments to the specification, and drawings add no new subject matter and their entry is respectfully requested.

In view of the above remarks and amendments, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent at (240) 453-3628 should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,
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